

# Translation

## PATENT COOPERATION TREATY

PCT/JP2004/002238



# PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference <b>FS04-408PCT</b>	FOR FURTHER ACTION See Form PCT/IPEA/416	
International application No. <b>PCT/JP2004/002238</b>	International filing date (day/month/year) <b>25 February 2004 (25.02.2004)</b>	Priority date (day/month/year) <b>26 February 2003 (26.02.2003)</b>
International Patent Classification (IPC) or national classification and IPC <b>C07K 14/47, C12N 15/12, A61K 37/02, A61P 35/00</b>		
Applicant <b>JAPAN SCIENCE AND TECHNOLOGY AGENCY</b>		

- This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
- This REPORT consists of a total of 6 sheets, including this cover sheet.
- This report is also accompanied by ANNEXES, comprising:
  - ☒ (sent to the applicant and to the International Bureau) a total of 4 sheets, as follows:
    - ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
    - ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
  - ☒ (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) Disc 1, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

- This report contains indications relating to the following items:

- ☒ Box No. I Basis of the report
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

Date of submission of the demand <b>18 May 2004 (18.05.2004)</b>	Date of completion of this report <b>13 January 2005 (13.01.2005)</b>
Name and mailing address of the IPEA/JP	Authorized officer
Facsimile No.	Telephone No.

# INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

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Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

- ☐ This report is based on translations from the original language into the following language \_\_\_\_\_, which is language of a translation furnished for the purpose of:
- ☐ international search (under Rules 12.3 and 23.1(b))
  - ☐ publication of the international application (under Rule 12.4)
  - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on (replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):

- ☐ The international application as originally filed/furnished
- ☒ the description:
- pages \_\_\_\_\_ 1-5,7,10 \_\_\_\_\_, as originally filed/furnished
- pages\* \_\_\_\_\_ 6,8,9 \_\_\_\_\_ received by this Authority on \_\_\_\_\_ 18 May 2004 (18.05.2004)
- pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- ☒ the claims:
- pages \_\_\_\_\_, as originally filed/furnished
- pages\* \_\_\_\_\_, as amended (together with any statement) under Article 19
- pages\* \_\_\_\_\_ 1-3,5-7 \_\_\_\_\_ received by this Authority on \_\_\_\_\_ 18 May 2004 (18.05.2004)
- pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- ☒ the drawings:
- pages \_\_\_\_\_ 1-7 \_\_\_\_\_, as originally filed/furnished
- pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- ☒ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☒ The amendments have resulted in the cancellation of:

- ☐ the description, pages \_\_\_\_\_
- ☒ the claims, Nos. \_\_\_\_\_ 4 \_\_\_\_\_
- ☐ the drawings, sheets/figs \_\_\_\_\_
- ☐ the sequence listing (specify): \_\_\_\_\_
- ☐ any table(s) related to sequence listing (specify): \_\_\_\_\_

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages \_\_\_\_\_
- ☐ the claims, Nos. \_\_\_\_\_
- ☐ the drawings, sheets/figs \_\_\_\_\_
- ☐ the sequence listing (specify): \_\_\_\_\_
- ☐ any table(s) related to sequence listing (specify): \_\_\_\_\_

\* If item 4 applies, some or all of those sheets may be marked "superseded."

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

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## Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
- ☒ claims Nos. 5-7

because:

- ☒ the said international application, or the said claims Nos. 5-7 relate to the following subject matter which does not require an international preliminary examination (*specify*):

The subject matters of claims 5-7 relate to a therapeutic method for cancer, hence a method for treatment of the human body by surgery or therapy and a diagnostic method, which do not require an international preliminary examination by the International Preliminary Examining Authority.

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. \_\_\_\_\_ are so unclear that no meaningful opinion could be formed (*specify*):

- ☐ the claims, or said claims Nos. \_\_\_\_\_ are so inadequately supported by the description that no meaningful opinion could be formed.

- ☐ no international search report has been established for said claims Nos. \_\_\_\_\_

- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

- ☐ has not been furnished

- ☐ does not comply with the standard

the computer readable form

- ☐ has not been furnished

- ☐ does not comply with the standard

- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

- ☐ see Supplemental Box for further details.

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**Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. Statement**

Novelty (N)	Claims	1-3	YES
	Claims		NO
Inventive step (IS)	Claims	1-3	YES
	Claims		NO
Industrial applicability (IA)	Claims	1-3	YES
	Claims		NO

**2. Citations and explanations (Rule 70.7)**

Document 1: "Genes Controlled by Transcription Factor P53 (in Japanese)," (Hirofumi Arakawa, et al.), Saibo-Kogaku (= Cell Technology), 22 December, 2002 (22.12.02), Vol. 22, No. 1, 2003, pages 23-28

Document 2: "Control of Cell Functions by Phosphorylation and Acetylation of p53 (in Japanese)," (Yoichi Taya), 22 December, 2002 (22.12.02), Vol. 22, No. 1, 2003, pages 29-33

Document 3: "Overexpression of O-linked N-Acetylglucosamine Transferase (OGT) Triggers Apoptosis," (S. Shin, et al.), Molecular Biology of the Cell, 2002, Vol. 13, Supple., 304a-305a, 1712

Document 4: "Controlled Elimination of Clathrin Heavy-Chain Expression in DT40 Lymphocytes," (F. R. Wetley, et al.), Science, 2002, Vol. 297, pages 1521-1525

Document 5: "p53AIP1, a Potential Mediator of p53-Dependent Apoptosis, and Its Regulation by Ser-46-Phosphorylated p53," (K. Oda, et al.), Cell, 2000, Vol. 102, pages 849-862

The subject matters of claims 1-3 appear to be novel and to involve an inventive step in view of documents 1-5.

Document 1 describes that (1) if Ser46 of transcription factor p53 is phosphorylated, cancer cells cause apoptosis, (2) mutants of p53 in which Ser46 is substituted by Phe significantly induce apoptosis in various carcinomas, and (3) these transcription factors are used for cancer therapy.

Document 2 describes that if Ser46 of transcription factor p53 is phosphorylated, apoptosis of cells is induced.

Document 3 describes that (1) overexpression of OGT triggers apoptosis, and (2) OGT makes N-acetylglucosamine bound to the serine residues and threonine residues of both control proteins (transcription factors such as p53) and structural proteins (clathrin assembly protein AP3, etc.).

Document 4 describes that a bird-derived cell obtained by inactivating the natural clathrin gene and introducing a human-derived clathrin heavy-chain cDNA was used to inhibit the expression of human-derived clathrin, for causing apoptosis.

Document 5 describes p53AIP1 gene, the expression of which is induced by p53, and also describes that (1) if the said gene is expressed, apoptosis is caused, (2) if Ser46 of p53 is phosphorylated, apoptosis is induced, (3) if Ser46 is substituted, the capability of p53 to cause apoptosis is inhibited, and (4) the expression of p53AIP1 is selectively inhibited.

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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.  
Continuation of: V

However, documents 1-5 neither describe nor suggest the effect that apoptosis in cancer cells can be enhanced if HC of clathrin is used together with p53 or any of its mutants (the effect shown in Fig. 9 of the present application). This constitution is not considered to be obvious to a person skilled in the art either.